PHARMA DEVILS

REPORT FOR RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION

REPORT

FOR

RISK ASSESSMENT & MITIGATION

PROCESS VALIDATION

PRODUCT: Cefuroxime Axetil (Amorphous)

STUDY OF Cefuroxime Axetil (Crystalline)
to Cefuroxime Axetil (Amorphous)

Facility: ……

LOCATION: ……

Document No.	
Protocol No.	
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REPORT FOR RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION

REPORT Contents

1. Report Approval

This is a specific Report for Risk assessment and Mitigation of Process Validation Study of Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous)which has been carried out in Plant This report has been prepared, reviewed and approved by following

Prepared By:

Name	Designation	Department	Signature	Date
		Quality Assurance		

Reviewed By:

Name	Designation	Department	Signature	Date

Approved By:

Name	Designation	Department	Signature	Date

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2.0 Overview

2.1 Objective:

The Objective of this Report is to adopt a systematic process for the assessment, control, communication and review of risk associated with the Process Validation Study Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous) which is carried out in the Plant.

2.2 Purpose and Scope

The purpose of this Report is to outline a scientific and practical approach for decision making process by applying a suitable tool of risk assessment covering all aspects of risk associated with Process Validation Study of Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous)

2.3 Risk Assessment Team

- Production Executive/Officer/Manager
- Quality control Executive/Officer/Manager
- Maintenance Executive/Officer/Manager
- Quality Assurance Executive/Officer/Manager

2.4 Responsibility

S.No.	Department	Designation	Responsibility
1.	Production	Executive /Officer / Manager	Review of Protocol & report To Provide the all relevant information that are required while undergoing Risk assessment process i.e. Quantity, Packaging etc.
2.	Quality control	Executive /Officer / Manager	Review of Protocol & report To Provide information about the availability of Analytical methods Pharmacopeia reference and finally reviewing the testing procedures

3.	Maintenance	Executive /Officer / Manager	Review of Protocol & report To assist the risk assessment team about the technical queries of facility & equipment's
4.	Quality Assurance	Executive /Officer / Manager	Preparation of Protocol & report To review all the Procedural controls both in-house and vendor To conduct audits to assess the quality management system and manufacturing facility Final approval of Protocol & report by head quality Assurance

3.0 Process Flow Diagram : Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous)

Cefuroxime Axetil (Crystalline)

Dissolution

Filtration

Spray Drying

Drying

Cefuroxime Axetil (Amorphous)

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4.0 Introduction

Risk analysis for Process Validation Study of Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous) has been performed by taking into the probability, occurrence and Severity. The risk is identified analyzed and evaluated. The risk identified analyzed and evaluated for Equipment's, Process, Raw Materials, and Process Parameters and in process Checks, Intermediate, and Impurities & Extraneous Matter.

4.1 Quality Risk Management Process

Risk assessment is a systematic process of organizing information to support a risk decision to be made within a risk management process. Its consists Identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.Quality risk assessment begins with a well-defined problem description or risk question.

For risk assessment process three fundamental questions are considered

- What might go wrong?
- What is likely hood **(Occurrence)** it will go wrong?
- What are the consequences **(severity)?**

- **Risk Identification**

Risk Identification is systematic use of information to identify hazards referring to risk questions or problem description. Information may include historical data theoretical analysis, informed opinions and concerns of stakeholders. risk Identification will be conducted by reviewing the types of events that might occur in both normal and unusual situations. This may be done by challenging the normal presumptions, and considering the possibilities of unanticipated situations. For each risk event, the underlying (root) cause should be determined that will create the potential risk occurrence.

Risk Identification addresses the "what might go wrong" question including identifying the possible consequences. This provides the basis for the further steps in quality risk management process.

- **Risk Analysis**

Risk analysis is the estimation of risk associated with the identified hazards.

It is the quantitative or qualitative process of linking the likelihood of occurrence and severity of harm and sometime the detectability of harm is also consider during estimation of risk.

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- **Risk Evaluation**

  Risk Evaluation compares the identified and analyzed risk against the given risk criteria. Risk evaluation considers the strength of evidence for all three of fundamental questions.
  Risks are ranked by scoring various criteria with appropriate numerical ratings, adding to scores to determine the overall score of each risk, and sorting the risks into descending order based on each score. A risk scoring threshold is established, over which risks must be mitigated using adequate design and/ or process controls that will protect the system. Those risks that fall below the threshold are either unmitigated or scheduled for later mitigation. An additional threshold or characteristic of risk can be used to determine the differentiation of non- mitigation versus postponed mitigation.

- **Risk Control**

  Risk control includes decision making to reduce or mitigate risk. The purpose of risk control is to reduce the risk to the acceptance level
  The risk control is done by considering the following question

  – Is the risk above an acceptable level?
  – What can be done to reduce or eliminate risk?
  – What is appropriate balance among benefits, risks and resources?
  – Are new risk is introduced as a result identified risk being controlled?

- **Risk Reduction**

  Risk reduction focuses on processes the mitigation or avoidance of quality risk when it exceeds the acceptable level. Risk reduction includes action taken to mitigate the severity, occurrence or probability of harm and the processes that improve the detectability of harm. It is the part of risk control strategy and involves

  – Engineering Control
  – Procedural Control
  – Manual control etc.

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4.2 Risk Assessment Legend

A. Severity

Ranking	Effect	Criteria
10	Hazardous	Hazardous effect without warning. Safety related. Regulatory non-compliant.
9	Serious	Potential hazardous effect. Able to stop without mishap. Regulatory compliance in jeopardy.
8	Extreme	Item inoperable but safe. Customer very dissatisfied.
7	Major	Performance severely affected but functional and safe. Customer dissatisfied.
6	Significant	Performance degraded but operable and safe. Non-vital part inoperable. Customer experiences discomfort.
5	Moderate	Performance moderately affected. Fault on non-vital part requires repair. Customer experiences some dissatisfaction.
4	Minor	Minor effect on performance. Fault does not require repair. Non-vital fault always noticed. Customer experiences minor nuisance.
3	Slight	Slight effect on performance. Non-vital fault notice most of the time. Customer is slightly annoyed.
2	Very Slight	Very slight effect on performance. Non-vital fault may be noticed. Customer is not annoyed.
1	None	No effect.

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B. Probability or Occurrence

Ranking	Possible Failure	Probability of Failure
10	≥1 in 2	Almost certain.
9	1 in 3	Very high.
8	1 in 8	High.
7	1 in 20	Moderately high.
6	1 in 80	Medium
5	1 in 400	Low
4	1 in 2,000	Slight
3	1 in 15,000	Very slight.
2	1 in 150,000	Remote.
1	1 in 1,500,000	Almost impossible.

C. Detection

Ranking	Detection	Likelihood of Detection by design control
10	Absolute Uncertainty	No design control or design control will not detect potential cause
9	Very Remote	Very remote chance design control will detect potential cause.
8	Remote	Remote chance design control will detect potential cause.
7	Very Low	Very low chance design control will detect potential cause.
6	Low	Low chance design control will detect potential cause.
5	Moderate	Moderate chance design control will detect potential cause.
4	Moderately High	Moderately high chance design control will detect potential cause.
3	High	High chance design control will detect potential cause.
2	Very High	Very high chance design control will detect potential cause.

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1	Almost Certain	Almost certain that the design control will detect potential cause.

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4.3 Risk Assessment Tool – Failure Mode effect Analysis (FMEA)

4.3.1 Risk Identification

Risk assessment team shall identify all possible failure modes of Process Validation of Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous) by reviewing the various aspects of facility design & operational features, Provisions and Adopted procedures. The risk identification involves three aspects

1. **Identification of Failure Mode of Process Validation Study of** Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous)
    a. Equipment
    b. Raw Materials
    c. Process (including In process & Intermediate)
    d. Equipment Cleaning
    e. Sampling, Handling & Testing
    f. Holding of Intermediate
    g. Mix-up
    h. Packing & Storage of the Product
    i. Environment of the Plant.
2. **Identification of Potential cause**
    a. Operator Error
    b. Equipment Malfunctioning
    c. Instrument malfunctioning
    d. Non availability or Non rational Procedures
    e. Inefficient Provisions for operations etc.
3. **The consequences i.e. End results of failure mode**
    The failure Mode may leads to
    a. GMP Violation
    b. Product Quality
    c. Patient
    d. Contaminated Product
    e. Regulatory non compliance
    f. Product Recall
    g. Unsafe operating conditions

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The identification done for the risk shall have scientific rational and must be justified for its validity. The below mentioned table shall be used for Risk Identification process.

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S. No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
	Risk Identification			

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01	**Equipments** Reactors	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Product Failure GMP Violation Contamination Deviation Impact on Conversion of reaction Yield Loss	Qualified equipments are used in production of Cefuroxime axetil (Crystalline) to Cefuroxime Axetil (Amorphous). Awarness provide through training and preventive maintenance records verified. Equipments history checked no malfunctioning was found. The equipment used in Cefuroxime Axetil (Amorphous) are SS reactors, Close Loop Spray Dryer, Rotary Vacuum Dryer (RVD), Multi mill The SS reactor (PE/SSR/001, PE/SSR/002) was used for mixing. The reactor is suitable for reaction as justified according the process Requirement. Close Loop Spray Dryer PE/LSD/001was used for drying operation was use for drying operation and achieves the LOD. It is concluded that all equipments which are used in the processing of Cefuroxime Axetil (Amorphous) are fulfill the process Requirement.

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S. No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
Risk Identification				
02	**Process**	Technology transfer Product stability Product knowledge Analytical method validation	Product validation Stability Filling Customer commitment Business impact Campaign failure	Cefuroxime Axetil (Amorphous) was develop in R&D. The R&D batches are kept on Holding Time Study. Based on ROS and process package development batches are taken batches were comply with the Specification After development batches evolution of quality and yield performed. Based on success of development batches the validation batches had been taken. All the batches comply with the specification. Based on R&D lab batches, Development batches and validation batches it is concluded that process is robust.

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
Risk Identification				
03	**Raw Materials**	Vendor Sampling Testing and specification Awareness Material handling and storage	Quality Product Failure GMP Violation Conversion of reaction Yield	Awareness regarding sampling, testing and handling of raw material provided. Material procured from approved vendors. Vendors were qualified as per SOP on vendor management. Raw materials are tested as per approved specification. Only approved raw materials are used in manufacturing of Cefuroxime Axetil (Amorphous). MSDS was followed for handling, sampling and storage of raw materials. Batches are taken as per Approved BPRs. All the in process parameter comply with specification. All the batches comply with the specification. Yield of all the batches was within range. Based on the yield, quality, in process check good laboratory practices and cGMP. It is concluded that the raw materials are of good quality and handled concluded that the raw materials are of good quality and handled sampled and tested appropriately

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
Risk Identification				
04	**Process Parameters and In process Checks**	Awareness Written Procedure Selection of Equipment's Raw Materials Sampling & Handling	Deviation Product Failure Yield Contamination	All the batches are taken as per approved BPR's.inprocess checks are defined in BPR's.Sampling and testing performed as per specification. Critical parameters were performed as per BPR's and Checked by Shift In charge. All the critical process parameters are identified as per process package of Product. Identified in BPR marked as Bell. Based on In process check. Critical parameters controlling on all the batches. Quality and quality are within limit. Parameters controlling on all the batches. Quality and quality are within limit.

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S. No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences (Severity)	Justification
Risk Identification				
05	**Impurities**	Raw Material Awareness Equipments Selection Batch size Analytical Procedure	Product Failure Product Contamination Deviation Yield and Quality	Structure elucidation had been performed at R&D. Analytical procedure are developed and apply. On all R&D Batches. Based on R&D Batches technology and Method Transferred of Cefuroxime Axetil (Amorphous).for Commercial Scale. All the batches comply with impurity profile by HPLC. Awareness provided before starting the campaign. Equipment's are selected keeping in observation of Impurities generation and heating cooling impact. Based on Evaluation of quality and yield data all the batches of Cefuroxime Axetil (Amorphous). That batches are taken in suitable equipment's under the supervision of trained man power

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06	**Extraneous Matter**	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Raw Material Packing Material Equipment Surface Floor & Walls of the facility	Cefuroxime Axetil (Amorphous).Manufactured in PE Block. All the raw material charged using PPE. Before charging of batch equipment surfaced is cleaned. The Floor and Walls of the facility are good condition.

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7.1	**Man Movement** **Case 1** Outside to Inside of the Plant	Apparels a source of Dust or Extraneous Matter Carrier Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person Inefficient provisions to remove Extraneous Matter from apparels of the entering Man	Extraneous Matter Entered as a result of Man entry inside the plant can contaminate the 1. Raw Materials 2. Packing material 3. Finished product 4. Equipment Surfaces 5. Floors & Walls of the facility	Person entering the plant performs different operations like 1. Handling of Material 2. Equipment operations 3. Cleaning 4. Processing 5. Packing etc. Person coming from out side, as source of Extraneous matter leads to contamination while performing above mentioned activities

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	Material Movement **Case 2** Material flow from Uncontrolled area to Controlled area	Non Availability of Standard Procedure and Provisions for the Material movement to the control area from uncontrolled area People are Not trained for the material flow procedures Insufficient Pressure gradient to prevent the flow of Extraneous Matter inside the control area Inappropriate door Opening and Closing Non availability of Cleanliness Verification Procedures before transferring the material to controlled area	Extraneous Matter Entered as a result of Material transfer inside the controlled area can contaminate 1. Packing material 2. Finished product 3. Equipment Surfaces 4. Floors & Walls of the Controlled Area	The transferring material to controlled area if not handled properly can become a source of Extraneous matter and can leads to contamination during Material handling Material unpacking Material holding etc.

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	Man Movement **Case 3** Man Exit (From Inside of the manufacturing Plant to Outside Area)	Non Availability of provisions to prevent the Exposure of internal environment to external environment Inappropriate door Opening and Closing	Man Exit from the Plant can leads to the extraneous matter incursion while opening and closing the doors	Inappropriate door opening & Closing give a chance for the Extraneous Matter incursion inside the facility which there after can move into the Material flow line and results into contamination

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7.2	**Air circulation** Failure of Air Handling Unit for the manufacturing facility	AHU System not Qualified Failure of Filter Integrity Un cleaned Return risers Disturbed Air balancing Disturbed Air Flow Pattern Failure of HEPA filters Non availability of standard operating procedure and provisions for AHU Systems Non availability of Preventive maintenance procedures for AHU System	Product Contamination Facility & Equipment Contamination with Extraneous Matter	Un Qualified AHU system cannot ensure its consistent performance Ruptured filters on the supply line of AHU system allow the particles to enter in the manufacturing area and leads to product contamination Disturbed Airflow pattern can result in the air stagnation inside the plant which can result into the extraneous matter accumulation. Disturbed air Balancing cannot maintain required pressure gradient between different areas of the facility Non availability of SOPs for operation and preventive maintenance leads to poor performance of AHU System

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4.3.2 Risk Analysis

Risk Analysis is the second step of risk identification Process. It involves the assessment of the

1. Severity of the Consequence of failure Mode
2. The Probability or Occurrence of Failure mode by reviewing effectiveness of the existing Design control
3. its detectability under the existing design control

Base upon the analysis Risk priority number will be assigned to the particular failure Mode as per the formula

RPN = Severity X Occurrence X Detection

Each index ranges from 1 (lowest risk) to 10 (highest risk). The overall risk of each failure is called Risk Priority Number (RPN) and the product of Severity (S), Occurrence (O), and Detection (D) rankings: RPN = S × O × D. The RPN (ranging from 1 to 1000) is used to prioritize all potential failures to decide upon actions leading to reduce the risk, usually by reducing likelihood of occurrence and improving controls for detecting the failure

The below mentioned table shall be used for Risk Analysis process

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4.3.2 Risk Analysis

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	Probabili...	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							Risk valuation

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01.	Equipment's Reactors	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Product Failure GMP Violation Contamination Deviation Impact on Conversion of reaction Yield Loss	Qualified equipment's (DQ,IQ,OQ,PQ) Preventive Maintenance of Equipment's Training to concerned persons Work order system to rectify any breakdown of equipment's	4	6	2	RPN = 4X6X2 = 48

S.No.	**Failure Mode {What can go wrong}**	**Potential cause of Failure**	**What are the Consequences**	**Existing Design Control**	**Severity**	**Probability**	**Detection**	**Risk Priority Number**
					(S)	**(P)**	**(D)**	**RPN=S x P x D**
	Risk Analysis							**Risk valuation**

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02	Process	Technology transfer Product stability Product knowledge Analytical method validation	Product validation Stability Filling Customer commitment Business impact Campaign failure	Technology transfer documents are provided from R& D to plant Trained Operators w.r.t process Method Validated	2	6	2	RPN = 2X6X2 = 24

S.No.	**Failure Mode {What can go wrong}**	**Potential cause of Failure**	**What are the Consequences**	**Existing Design Control**	**Severity**	**Probability**	**Detection**	**Risk Priority Number**

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					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							**Risk valuation**
03	Raw Materials	Vendor Sampling Testing and specification Awareness Material handling and storage	Quality Product Failure GMP Violation Conversion of reaction Yield	SOP for dispensing of material Provision of PPEs SOP for cleaning of scoop and scrapers Trained Operators Procedure for the destruction floor sweep material Separate De-dusting facility are provided for both raw materials & packing materials MSDS are available w.r.t materials	2	6	2	RPN = 2X6X2 = 24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number RPN=S x P x D
	Risk Analysis							**Risk valuation**
04	Process Parameters and In process Checks	Awareness Written Procedure Selection of Equipments Raw Materials Sampling & Handling	Deviation Product Failure Yield Contamination	Process design for filtration to prevent Extraneous matter incursion in the API like particle,rust etc (Ref Manufacturing BPRs) Procedural control to check the by visual inspection by sight glass & verification through BPR Instruction	2	6	2	RPN = 2X6X2 = 24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	[illegible]	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							**Risk valuation**
05	Impurities	Raw Material Awareness Equipment's Selection Batch size Analytical Procedure	Product Failure Product Contamination Deviation Yield and Quality	Specification & STP are provided to analyst Qualified Instrument are Method Validation are provided to analyst Provision of PPEs Trained analyst	4	6	2	RPN = 4X6X2 = 48

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	.	.	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D
	Risk Analysis							**Risk valuation**
06	Extraneous Matter	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Raw Material Packing Material Equipment Surface Floor & Walls of the facility	Work order system to rectify the failure of door functioning Air curtains are installed on the entry doors for the plants The SOP to verify personnel hygienic which allows verification through checklist for cleanliness for the operating persons	5	6	2	RPN = 5X6X2 = 60

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	What are the Consequences	Existing Design Control	Severity	Probability	Detection	Risk Priority Number
					(S)	(P)	(D)	RPN=S x P x D
7.1	**Man Movement** **Case 1** Outside to Inside of the Plant	Apparels a source of Dust or Extraneous Matter Carrier Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person Inefficient provisions to remove Extraneous Matter from apparels of the entering Man	Extraneous Matter Entered as a result of Man entry inside the plant can contaminate the 1. Raw Materials 2. Packing material 3. Finished product 4. Equipment Surfaces 5. Floors & Walls of the facility	The Standard Procedure to verify personnel hygiene which allows Verification through checklist for Cleanliness for the operating persons Work order system to rectify the failure of door functioning Air curtains are installed on the Entry doors for the plants	7	4	2	=7 x 4 x 2=56

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7.2	**Man Movement** **Case 2** Uncontrolled Area to Controlled Area	Non Availability of Standard Procedure and Provisions for the Man movement to the control area from uncontrolled area People are Not trained for the Entering Procedures Insufficient Pressure gradient to prevent the flow of Extraneous Matter inside the control area Inappropriate door Opening and Closing	Extraneous Matter Entered as a result of Man entry inside Controlled area can contaminate 1. Packing material 2. Finished product 3. Equipment Surfaces 4. Floors & Walls of the Controlled Area	Standard operating procedure for the Entry & Exit to the controlled area of the plant (gowning procedures) Photo Display for the gowning procedures and verification of dress up for its exactness Training is Provided for all personnel for the Entry procedures Standard procedures for Environment monitoring of powder processing Area which regulates Differential pressure monitoring in each shift Double Airlock Provision for entering into the controlled area Work order system to rectify the failure of door functioning	7	4	2	=7 x 4 x 2=56

4.3.3 Risk Reduction or Mitigation

The Risk Reduction or Mitigation is the Third step of Risk assessment process if the Existing design control cannot lead the risk priority number to the acceptable level then additional design control shall be worked by providing

1. New or Improved Provisions or Procedures
2. Modification in the existing facility design
3. Additional resources
4. Improved control strategy etc.

   The additional design control shall be appropriately worked out to reduce the risk to its acceptable level. The below mentioned table shall be used for the Risk Reduction or Mitigation process

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4.3.3 Risk Reduction or Mitigation

S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
1.	Equipment's (Reactors and Centrifuge)	Equipment Selection Equipment Qualification Man hole Opening & Closing Awareness Equipment Malfunctioning Power failure	Qualified equipment's (DQ,IQ,OQ,PQ) Preventive Maintenance of Equipment's Training to concerned persons Work order system to rectify any breakdown of equipment's	4	6	2	48	Existing design control keep the risk at acceptable level.	4	6	2	48

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
02	Process	Technology transfer Product stability Product knowledge Analytical method validation	Technology transfer documents are provided from R& D to plant Trained Operators w.r.t process Method Validated	2	6	2	24	Existing design controls keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
03	Raw Materials	Vendor Sampling Testing and specification Awareness Material handling and storage	SOP for dispensing of material Provision of PPEs SOP for cleaning of scoop and scrapers Trained Operators Procedure for the destruction floor sweep material Separate De-dusting facility are provided for both raw materials & packing materials MSDS are available w.r.t materials	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
4.	Process Parameters and In process Checks	Awareness Written Procedure Selection of Equipment's Raw Materials Sampling & Handling	Process design for filtration to prevent Extraneous matter incursion in the API like particle, rust etc (Ref Manufacturing BPRs) Procedural control to check the Layer separation by visual inspection by sight glass & verification through BPR	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
5.	Intermediate	Sampling, Testing Material handling and storage	Specification & STP are provided to analyst Trained analyst	2	6	2	24	Existing design control keep the risk at acceptable level.	2	6	2	24
6.	Impurities	Raw Material Awareness Equipment's Selection Batch size Analytical Procedure	Specification & STP are provided to analyst Qualified Instrument are Method Validation are provided to analyst Provision of PPEs Trained analyst	4	6	2	48	Existing design control keep the risk at acceptable level.	4	6	2	48

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S.No.	Failure Mode {What can go wrong}	Potential cause of Failure	Existing Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)	Additional Design Control	Severity (S)	Probability (P)	Detection (D)	Risk Priority Number (RPN)
	Risk Mitigation											
7.	Extraneous Matter	Inappropriate door Opening &Closing Non Availability of Standard Procedure for cleanliness verification of entering person	Work order system to rectify the failure of door functioning Air curtains are installed on the entry doors for the plants The SOP to verify personnel hygienic which allows verification through checklist for cleanliness for the operating persons	5	6	2	60	Existing design control keep the risk at acceptable level.	5	6	2	60

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5.0 Acceptance Criteria

The Risk Priority Number shall be within the range 0<RPN<100

6.0 Risk Control Strategy

S.No.	Risk Priority Number	Risk Decision	Risk control strategy
1.	0<RPN<100	Risk Acceptable	No control is required
2.	100<RPN<500	Risk Reduction	Additional Procedural Control
			Manual Control
			Documentary Evidence
3.	500<RPN<1000	Risk Reduction	Rugged Procedural control
			Additional Manual Control
			Auditing
			Engineering controls (if Possible)

7.0 Summary and Conclusion

The Risk assessment of Cefuroxime Axetil(Amorphous) Product had been performed taking in to consideration Manual operations, operator involvements, cross contamination and handling of hazardous materials. Risk has been evaluated and found risk priority number below 100.

As per protocol if RPN is less than 100 risk is acceptable. maximum 60.Hence it is concluded that based on risk analysis that risk is acceptable.

As all the personnel are qualified & trained, equipment's are qualified.Batches are taken as approved BPR. All the critical Process Parameter has been identified. There is no product failure, no deviation found during manufacturing of Cefuroxime Axetil (Amorphous).

Hence Risk is LOW & is below 100.The report has been prepared by evaluating all possible risks and finally approved by Quality Assurance head.

8.0 Report Approval.

The report has been prepared by evaluating all possible risks and finally approved by Quality assurance head.

9.0 References and attachments:

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REPORT FOR RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION

Risk Management Master Plan (RMMP)
ICH Q9

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Annexure – 01

List of Reference Documents

Facility :	
Location:	
No. of Pages:	

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REPORT FOR RISK ASSESSMENT & MITIGATION FOR PROCESS VALIDATION

List of reference documents

S.No.	Document Title
1.	SOP on Vendor Assessment, Evaluation and Approval
2.	SOP on Prepration,Control,Issuance and Revision of Batch Production Records and Batch Records for cleaning
3.	SOP on Document and Data Control
4.	SOP on Change Control Procedure
5.	Approval and Release of Finished goods / intermediate.
6.	SOP on Labeling of Raw Material, Packing Material, Intermediate and Finished API
7.	SOP on Procedure on Handling of Deviation
8.	SOP on Batch Numbering System
9.	SOP on Technology Transfer
10.	SOP on Handling of Customer Complaints
11.	SOP on Equipment Qualification and Validation of System and Process
12.	Rectification of Errors
13.	SOP on Procedure for Training of Employees
14.	SOP for Personal Hygiene of Employees
15.	Recruitment of employee
16.	SOP for Calibration of Reactor, Receiver and Tank
17.	SOP on Operation of Scrubber
18.	SOP on Issuance, Usage and Disposal of Centrifuge Bags
19.	SOP on movement of Dispensed Raw Material
20.	SOP on Disposal of Floor Swiping
21.	SOP on Receipt, Sampling, Testing, Approval & Rejection of Packaging Material
22.	SOP on Calibration & Preventive Maintenance of Laboratory Instruments
23.	SOP on Testing and Release of In-Process Samples
24.	SOP on qualification of Analysts
25.	SOP on Retention Samples of Critical raw Materials & Intermediates
26.	SOP on Passwords Protection and Audit Trail for critical QC Instruments
27.	SOP on Good Laboratory Practice